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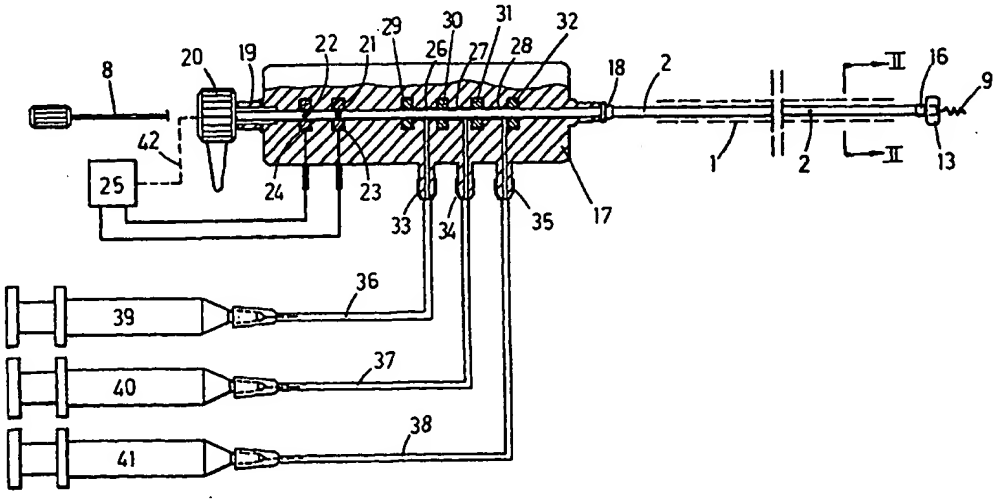

(57) Abstract

The multilumen catheter (2) is provided at one end with a needle system (9, 9') formed by two or more single–lumen needles which are provided with respective discharge openings (110, 111) and which, via their longitudinal lumina (10, 11), are connected to corresponding lumina (3, 4) of the catheter for separate release of a tracer fluid for external image diagnostics systems and therapeutic fluids, for example DNA plasmids. The needles may be both straight or both helical or one of these needles may be straight and the other needle may be helical.

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TITLE: Catheter system for performing intramyocardiac therapeutic treatment.

DESCRIPTION

The invention relates to a method and the associated apparatus for performing intramyocardiac therapeutic treatment by means of the controlled infusion, in this anatomical location, of therapeutic fluids of varying nature and composition. With this method and apparatus it is possible to treat patients who suffer from cardiac ischaemia and who are not able to tolerate surgical therapy involving a coronary bypass or coronary angioplasty using catheters. At present there are many patients suffering from heart disease which is advanced to the point where it can no longer be treated using the solutions mentioned. Complete re-vascularization is not possible in 20% of the patients who undergo bypass surgery. The patients who cannot be treated with the abovementioned solutions belong, for example, to the following categories: patients with extensive heart disease affecting the distal vessels; patients with symptomatic ischaemia resulting from a diseased vessel which is too small to be bypassed; patients who do not have adequate ducts for bypassing; patients with total chronic occlusion and with distal vessels which are small and/or cannot be viewed.

A new therapy which is currently becoming more widespread for the treatment of this type of patient consists in the percutaneous injection, into the cardiac muscle, of genic substances, for example DNA plasmids, which induce the formation of new blood vessels. At least six different carrier systems have been used for genic transfer to the heart muscle cells, namely: DNA devoid of viral or physical adjuvants which increase the genic release; DNA encapsulated in modified liposomes; DNA complexed with cationic liposomes; retroviral carriers; adeno-associated viral carriers. This therapy is currently performed by making a small incision in the chest in order to inject the abovementioned plasmids into the myocardium, continuously monitoring the patient by means of transoesophageal echocardiography in order to check the movement of the cardiac wall during the percutaneous injection, in order to prevent the plasmid being injected into the blood, inside the cavity of the left-hand ventricle. The recent clinical experiments involving injection of plasmids into the myocardium, during surgical treatment or a mini-

thoracotomy, are very interesting, but are unable to solve many problems when this procedure is used as the one and only therapy, in particular problems relating to optimization of the most suitable site for injection and the number and dosing of the intramyocardial injections. It is also obvious that the surgical solution limits very much the possibility of performing multiple treatment or treatment which is repeated over time.

It was thought that a catheter system suitable for the intramyocardiac injection of plasmids may be able to overcome the limitations of the present surgical solution indicated above.

According to the publication "Percutaneous Transluminal Gene Transfer into Canine Myocardium in Vivo by Replication-Defective Adenovirus" Jian Jun Li et. al. (Cardiovascular Research 1995; 30: 97-105), previous experiments involving the percutaneous injection of genes into the myocardium of dogs, by means of adenovirus, were performed using an injection catheter composed of a catheter guide and a guided catheter, with a needle at its terminal end, inserted into the left-hand ventricle of the heart. Under a fluoroscope, the needle was inserted into the myocardium and its correct position of insertion was confirmed by suction of the blood. If the needle is inserted into the wall of the cardiac muscle, its lumen is closed by the muscle itself and therefore the suction of blood is prevented.

Various injection catheters have been studied in order to improve the injection of a drug into an area inside the human body. Injection catheters have for example been produced by Wilson Cook Medical Inc. (Cook Italia Srl), said catheters being specifically designed for the sclerotherapeutic endoscopic treatment of oesophageal varices. The Boston Scientific Corporation markets needles for liquid injection therapy using a dedicated twin-lumen catheter and associated extendable and retractable needle with an ample washing lumen for ensuring vision with an endoscope in bleeding conditions.

None of the catheters with injection needles proposed by the current technology has been specifically developed and can neither be adapted to solve the problem of percutaneous and transvascular injection of plasmids into the human

myocardium. With a needle catheter of the known type it is difficult to maintain a fixed position inside the moving wall of the myocardium and it is therefore difficult to inject, in a reliable manner, plasmids into the said wall. Similar difficulties have been encountered with the catheters of pacemakers when they have to be positioned in a different point of the apex of the right-hand ventricle, for example in the interatrial or interventricular septum. In these cases, a helical electrode screwed into the wall of the endocardium, in order to ensure immediate stability of the implant pending the growth of tissue thereon, is used. The use of a helical and hollow electrode for the injection of liquids into the human body has been described in US Patent No. 5,431,649 for a purpose different from that of the present invention, namely for the hyperthermic treatment of neoplasia of the prostate and for treatment of myocardiac ablation by means of radiofrequency, using a perfusion of saline solution through the cavity of the helical electrode.

An important factor which prevents the use of the abovementioned catheter perfusion systems for the function in question is the fact that they are not able to provide a safe, reproducible and recordable method for demonstrating that the injection of the plasmids is performed in a selected area of the myocardium and not in the blood stream; in fact the aforementioned solution of confirming the position of the needle by suction is not suitable for this purpose on account of the high risk of false situations created by the closure of the needle lumen by blood clots.

A recent publication "Transcatheter Subendocardial Infusion. A Novel Technique for Mapping and Ablation of Ventricular Myocardium", Andreas Goette et. al. (Circulation 1996; 94: 1149-1455) described an infusion catheter equipped with an electrode corresponding to the injection needle located on the distal end of said catheter and provided with a second ring electrode in the vicinity of the same needle. Two lumina which are formed inside the catheter and by means of which it is possible to perform a sequential administration of fluid mixtures converge towards this needle. A tracer substance is injected via a lumen of the catheter in order to map, by means of fluoroscopy, the point of injection of the needle into the myocardium of the left-hand ventricle, while a fluid mixture with ethanol is

subsequently injected through the second lumen of the catheter in order to perform a chemical ablation of a volume of the myocardium. By means of this method, with the associated catheter, it is possible to identify with reasonable certainty the area of the myocardium into which the needle is inserted, but the problems, as described in the abovementioned publication, resulting from the difficulty of keeping a straight needle in the correct position in a beating myocardium and preventing remixing between the fluids introduced through the two catheter lumina, the latter intercommunicating via the common lumen of the injection needle, cannot be solved. Owing to the inherent elasticity of the material from which the lumina of the catheter may be made and the notable curvature to which the catheter itself is subject during insertion into the human body, it cannot be ruled out that the pressure exerted on a fluid which is to be injected may cause a partial transfer of this fluid from its lumen under pressure to the other lumen which is at a lower pressure, with the result of unexpected and constant mixing of the two fluids and possible limitation of the volume of the fluid actually injected into the myocardium, since a part of this fluid, instead of being discharged from the needle, flows back into the lumen of the catheter which is at a pressure less than that of the active lumen.

US Patent No. 5,354,279 ("Plural Needle Injection Catheter") envisages a catheter provided at its terminal end with a plurality of thin pre-formed metal needles emerging in a ray-like arrangement and designed to release pharmaceutical substances onto the arteries. The lumina of these needles communicate, however, with a single lumen of the catheter so that this apparatus may not be used for the purposes of the present invention, either.

By way of conclusion, the known art, with the procedures and the devices described based on a catheter system with injection needle, does not allow the practical realization of an apparatus and a method for injecting plasmids solely using the intramyocardiac method, owing to problems associated with the movement of the endocardium and the impossibility of separating completely injection of the therapeutic fluids from injection of the tracer fluid.

The object of the invention is to solve these and other problems of the

already known art by means of a catheter provided with two or more longitudinal lumina and provided at its terminal end with a multilumen needle system, each lumen of this needle system having its own discharge opening and being connected to a corresponding lumen of the catheter. The lumina of the catheter are connected to external systems for releasing separately tracer fluids for external image diagnostics systems by means of which it is possible to verify the correct position of the needle in the cardium tissue and release therapeutic fluids, for example DNA plasmids. The needle system in question may be formed by a multilumen needle or by several single-lumen needles arranged alongside each other and each connected to a corresponding lumen of the catheter.

Further characteristic features and advantages arising therefrom will appear more clearly from the following description of certain preferred embodiments thereof, illustrated purely by way of a non-limiting example in the accompanying sheets of drawings, in which:

- Fig. 1 is an overall side view, with parts shown in cross section, of the catheter system according to a preferred embodiment of the invention;

- Fig. 2 shows a cross section through the middle of the catheter, along the line II-II of Figure 1;

- Figs. 3 and 4 show further details of the end part of the catheter with a multilumen needle, which is sectioned respectively along the lines III-III and IV-IV of Figure 2 and with parts being visible;

- Fig. 3a is a variation of embodiment of the straight needle;

- Figs. 5 and 6 are cross sections through the multilumen needle along the lines V-V and VI-VI of Figure 3, respectively;

- Fig. 7 shows, longitudinally sectioned, the end part of a multilumen catheter, with the multilumen needle system being formed by two single-lumen and straight needles arranged alongside each other;

- Figs. 8 and 9 show possible cross sections through the needles of the needle system according to Figure 7, sectioned along the line VIII-VIII;

- Fig. 10 shows, cross sectioned and with parts visible, a needle system

formed by two straight and coaxial needles;

- Figs. 11 and 12 show details of the needle system according to Figure 10, sectioned along the lines XI-XI and XII-XII, respectively;

- Fig. 13 shows, cross sectioned and with parts visible, a needle system formed by two helical needles arranged alongside each other;

- Fig. 14 shows, cross sectioned and with parts visible, a needle system formed by two straight needles coaxial with each other and of different length and with the projecting needle portion having a helical shape;

- Figs. 15 and 16 show, cross sectioned and with parts visible, further needle systems formed by a straight axial needle circumscribed by a helical needle which may be, respectively, projecting or retracted with respect to the said axial needle.

In Figures 1 and 2 the numeral 1 designates schematically a catheter guide of the known type which is pre-formed or steerable and which is inserted into the blood circulation which leads to the left ventricle of the heart and inside which the catheter system in question is then inserted, said catheter system comprising a catheter 2 which has a suitable length and cross section and is made of any material suitable for this purpose, for example Polyimide, and is provided internally with a meshwork braiding 102 and/or other suitable means (see also Fig. 3) which allow a twisting torque to be applied to the said catheter, without the latter being deformed, such that a rotation applied to the front end of the catheter results in an identical rotation of the terminal end of this catheter. The catheter 2 is provided internally with several longitudinal lumina, for example a pair of main and opposite lumina 3 and 4, for example having a cross section in the form of a circle segment, and has between said lumina, in a symmetrical arrangement, arranged alongside each other and aligned along the diametral plane of the catheter, three secondary lumina 5, 6 and 7, for example with a round cross section, one of which is located preferably coaxially in the catheter, for receiving the guide spindle 8 which is of the type usually used for operating traditional pacing catheters.

A multilumen needle system is fixed onto the terminal end of the

catheter 2 by means of a special insert 12, in a position of longitudinal alignment with the said catheter, said needle system being formed by a needle which may be straight as indicated by 9' in Figure 3a or may preferably have a cylindrical helical shape, as indicated for example by 9 in Figures 3 and 4. It is understood that the scope of the invention also includes helical needles other than that illustrated, for example which are of the straight type and have one or more external helices, for example similar to wood screws. From Figure 5 it can be seen that the needle has two longitudinal lumina 10 and 11 which are arranged closely alongside each other and divided by a common wall 309 over the whole length of the body of this needle. The base of the needle has a fork-shaped configuration and the corresponding branches 109 and 209, which form a continuation of the respective lumina 10 and 11 of the said needle, are engaged in the corresponding lumina 3 and 4 of the catheter.

Both in the case of Figure 3 and in the case of Figure 3a, the internal lumina of the needle are provided with respective lateral discharge openings, one of which is indicated by 110 and is located at a short distance from the needle tip, while the other one indicated by 111 is located further upstream, in the middle part or at the base of the said needle (see also Figure 6).

The terminal end of the catheter is provided with a retractable device, which is useful as an end-of-travel stop, for stopping penetration of the needle 9 or 9' into the wall of the myocardium which has to be treated. For this purpose it may be possible to use a torus-shaped balloon 13 which is made of impermeable and flexible material and which is fixed laterally onto the terminal end of the catheter 2 and has at least one internal duct 113 which passes through the insert 12 and is designed to engage into one of the secondary lumina of the catheter, for example into the lumen 6 (Fig. 2).

From Figure 4 it can be seen that the end of an electrical conductor 14 which runs along the whole length of the catheter and is housed inside one of the secondary lumina, for example the lumen 7 in Figure 2, is connected to the body of the needle 9 or 9', together with an optional additional electrical conductor 15 connected to an optional ring 16 which is made of electrically conducting material

and is fixed on the outside of the terminal end of the catheter and is useful as a reference electrode for the various operations where the needle acts as a conductor of electrical impulses. The conductors 14 and 15 are suitably insulated from each other. If the braiding 102 of the catheter is made of an electrically conducting material, it may replace either one of the said electrical conductors 14 or 15. It is understood that the function of reference electrode may be performed by means other than the ring 16 mentioned above, for example using solutions known in the sector of cardiac electro-stimulation.

From Figure 1 it can be seen that the initial section of the catheter passes through the body of a distributor 17 with respect to which the said catheter may rotate, but not move axially, for example owing to the presence of end stops 18 and 19. The knob 20 by means of which a rotation may be imparted to the said catheter is fixed onto the front end of the catheter, whereas, with regard to that stated above, the distributor 17 may remain at a standstill. The front ends of the electrical conductors 14 and 15 are connected to small electrically conducting rings 21 and 22 which are fixed externally to different points of the catheter body, are insulated with respect to each other and with which brushes 23 and 24 of the distributor 17 co-operate, said brushes being in turn connected via respective conductors to a composite, external, fixed apparatus 25, which will be described in greater detail below.

The lumina 3, 4 and 6 of the catheter are closed at the outer front end and are provided along the section which passes through the distributor 17 with respective radial openings which are situated at mutually distant points of the catheter and lead into respective annular chambers 26, 27 and 28 of said distributor and which are insulated from each other and from the exterior by annular sealing gaskets 29, 30, 31 and 32. These chambers lead to cable connectors 33, 34 and 35 to which flexible pipes 36, 37, 38 may be connected, said flexible pipes being provided at the other end with Luer connectors to which syringes 39, 40, 41 may be connected, the first thereof being useful, for example, for injecting or drawing liquid into/from the balloon 13, i.e. for filling it and activating it as shown in Figure 4 or for

reducing it into the collapsed condition as shown in Figure 3, while the syringe 40 is useful for example for injecting tracer liquid which will emerge, for example, from the opening 111 of the needle 9 or 9', and the syringe 41 is used, for example, for injecting DNA plasmids which for example will be discharged from the end opening 110 of the said needle.

The catheter system as described functions and is used in the following manner. After positioning the catheter guide 1 in the patient, the catheter 2 is inserted inside said guide by means of the special guide spindle 8. The end balloon 13 is in the collapsed condition. After insertion of the catheter, the balloon 13 is activated by means of the syringe 39 and, by means of the external knob 20, the catheter itself is rotated in the direction for screwing of the helical needle 9 into the myocardium, until this needle has been completely screwed in. The correct position of the needle may be verified from the outside by means of the apparatus 25 which detects, for example, a bioelectrical impedance and/or ECG, using the electrical conductor 14 connected to the needle and the conductor 15 connected to the annular reference electrode 16. In order to improve the results of this test, the needle 9 or 9' may be advantageously lined with a thin layer of electrically insulating material, for example, Parylene, over practically the whole length, as schematically indicated by the broken lines and by 45 in Figures 3a and 4, except for an appropriate tip portion which remains electrically conducting.

Once screwing of the needle into the myocardium has been performed, via the syringe 40, a correct quantity of tracer is injected into this wall and, if the needle is correctly inserted, remains for a relatively long period of time in the said wall and may be easily detected by external image diagnostics systems of the known type, in the form of a persistent spherical-shaped mark. Should the needle not be correctly inserted into the myocardium, the injected tracer would become dispersed in the blood stream. The injected tracer may for example be of the type which is useful for detection by means of X-rays or using ultrasound image or magnetic nuclear resonance systems. If a dual-lumen needle as shown in Figures 3 and 3a is used, the tracer fluid is preferably discharged from the orifice 111 of the needle itself

since, if it is subsequently established using the abovementioned procedure that the needle is correctly inserted in the myocardium, there is the absolute certainty that the other discharge orifice 110, intended for the discharge of therapeutic fluid, is also correctly inserted into the myocardium itself.

After verifying and documenting with appropriate means that the needle has been correctly inserted, DNA plasmids are injected into the myocardium via the syringe 41. In order to reinforce the transfer of the abovementioned plasmids into the cells of the cardiac tissue, the external apparatus 25 may be arranged so as to transmit into the tissue itself, via the electrical circuit connected to the needle 9, electrical impulses which have suitable characteristics and are synchronized with the beat R of the spontaneous activity of the heart. Again for this purpose, the external apparatus 25 may be designed to generate ultrasounds which are conveyed to the needle 9 and therefore to the perfused zone of the myocardium, via a conductor with suitable characteristics, which is indicated schematically in Figure 1 by 42 and which is for example connected to the needle via the axial lumen 5, after removal of the guide spindle 8. It is understood that the catheter may have a secondary lumen specifically designed to contain an ultrasound conductor connected to the needle 9 or 9'.

With reference to Figures 7 to 16, variations of embodiment of the needle system mounted on the catheter will now be described, said catheter, unlike the one previously considered, being composed of two single-lumen needles. The catheter 2 illustrated in Figure 7 is identical to the multilumen catheter illustrated in Figure 1 and its lumina 3 and 4, which are respectively connected to the external systems for injection of the therapeutic fluid and the tracer fluid, are joined to the end sections 109, 209 of respective straight and single-lumen needles 9'a and 9'b which are preferably of different length, preferably arranged in axial alignment with the catheter and preferably fixed together by means of welds 43, as can be seen from Figure 8. 10 and 11 indicate the lumina of the needles which terminate in respective openings 110, 111 for discharging the fluids conveyed by said lumina. The tip of the shorter needle is preferably shaped in the manner of a flute mouth-piece and is

suitably connected to the side surface of the adjacent needle in order to facilitate penetration, into the myocardium, of the needle system 9' thus formed. Figure 9 illustrates a variation according to which the needles 9'a and 9'b have a flattened - for example semi-circular - cross section so that the needle system 9' formed by them can be made to assume a substantially round cross section.

In the solution according to Figures 10, 11 and 12, again relating to a needle system 9' of the straight type, the longer needle 9'a is partly inside and coaxial with the shorter needle 9'b, the end part of which is closed, converging onto the needle 9'a, and may be provided with several lateral openings 111 for discharging the tracer fluid. The needle 9'a emerges in a sealed manner from the needle 9'b at the start of the bifurcation which forms the end sections 109 and 209 for connection to the lumina 3 and 4 of the catheter.

The solution according to Figure 13 is equivalent to that of Figure 7, but envisages a needle system 9 which is formed by two helical needles 9a and 9b which are arranged alongside each other and preferably fixed by means of welding and which extend around the axis of the catheter 2. The comments made with reference to Figures 8 and 9 for the solution of Figure 7 are also applicable here. The needles enter preferably into the catheter being closely arranged around its axis and then diverge away from each other and engage into the lumina 3, 4 with the end sections 109, 209. It is understood that the scope of the invention also includes the variant, not shown, whereby the helical needles 9a and 9b are staggered and distant from each other, with the tip of the shorter needle being distant from the body of the longer needle. In this case the needles may enter into the catheter with sections which are distant from the axis of the said catheter.

The solution according to Figure 14 is derived from that of Figure 10 and envisages a needle system 9 formed by a short needle 9'b of the straight type from which a needle 9a terminating in a helical shape projects coaxially.

The solution according to Figure 15 illustrates a needle system 9 formed by a straight short needle 9'b which is aligned axially with the catheter and by a long helically shaped needle 9a which extends concentrically around the said

central needle 9'b.

The solution according to Figure 16 is a variation of the solution according to Figure 15 and envisages a needle system 9 formed by a long straight central needle 9'a and by a helically shaped external needle 9b which extends concentrically around the said central needle. This solution could be preferred to that of Figure 15 since the straight central needle 9'a is inserted firstly into the myocardium and acts as a centring element and a rotational pivot for the helical needle 9b. In both solutions according to Figures 15 and 16, the helical needle is able to enter into the catheter with an arrangement close to the straight needle, as illustrated by continuous lines, or is able to enter into the catheter with an arrangement offset from the axis of the straight central needle, as indicated by A and B, in order to favour, if necessary, automatic stopping of the screwing action of the needle system.

In Figures 7 to 16, 44 denotes in broken lines the location, if necessary, on the terminal end of the catheter, of an ultrasound generator which is integral with the base of one or both needles and connected to an electrical supply circuit, not shown, which passes through a secondary longitudinal lumen of the catheter for connection to an external power supply unit. With this solution it is possible to transmit to the needle system, and therefore to the perfused zone of the myocardium, the ultrasounds which are necessary for reinforcing the transfer of the therapeutic fluid into the cells of the myocardium tissue. It is understood that the same comments made in respect of the preceding solutions are applicable to the variations according to Figures 7 to 16, with regard to the possibility of electrical connection of the needle system to external apparatus and partial insulation of the said needle system, except for a suitable section of its terminal part, using electrical insulation material, for example based on "Parylene". The catheter will also be provided on the terminal end with the electrically conducting ring 16 having the function of a reference electrode for all the operations which the needle system performs as a conductor of electrical impulses. The catheter will also be provided with the internal anti-twisting braiding 102 and on the terminal end of the said

catheter the already mentioned retractable device 13, with external activation and deactivation controls, for stopping penetration of the needle system into the myocardium will be provided.

It is understood that the dimensions and the proportions indicated in the drawings are purely exemplary and do not limit the scope of the invention. Purely by way of a non-limiting example, some dimensional characteristics for the construction of the apparatus according to the invention are now described. The catheter 2 may, for example, have an external diameter of about 7 French, that is to say about 2.1 mm, while the external diameter of the helix of the needle system with at least one helical needle, may for example be about 2 mm. The projecting part of the longer needle must not, for example, exceed the length of about 5 mm, while the projecting part of the shorter needle will have for example a length of about 2.5 - 3 mm. The needles which form the needle system may for example each have an external diameter of about 0.30 mm.

CLAIMS

1. Catheter system, in particular suitable for performing intramyocardiac therapeutic treatment, of the type which comprises a hollow catheter body provided on its terminal end with a hollow needle for the injection of fluids through the said catheter, characterized in that:

- the body of the catheter (2) has two or more longitudinal lumina (3, 4) which are connected at one end to external means for administering fluids;

- the terminal end of the catheter is provided with a needle system (9, 9') having two or more longitudinal lumina (10, 11) with respective discharge openings (110, 111), the lumina of the needle system being connected to corresponding lumina (3, 4) of the catheter, in order to release separately a tracer fluid for external image diagnostics systems and therapeutic fluids, for example DNA plasmids.

2. Catheter system according to Claim 1, in which the end-needle system (9, 9') of the said catheter (2) consists of a multilumen needle.

3. Catheter system according to Claim 2, in which the multilumen needle is of the straight type.

4. Catheter system according to Claim 2, in which the multilumen needle is of the helical type.

5. Catheter system according to Claim 1, in which the end-needle system (9,9') of the catheter (2) is formed by two or more single-lumen needles, the longitudinal lumina (10, 11) of which are provided with respective lateral discharge openings (110, 111) and are connected via the bottom end sections (109, 209) to the corresponding lumina (3, 4) of the catheter.

6. Catheter system according to Claim 5, in which the needles which form

the needle system are of different lengths.

7. Catheter system according to Claim 5, in which the needle system (9') is formed by two straight needles (9'a, 9'b) of different length which are arranged along the axis of the catheter and fixed together with welds (43), the tip of the shorter needle (9'b) being suitably connected to the side surface of the longer needle (9'a).

8. Catheter system according to Claim 7, in which the needles have a flattened - for example substantially semi-circular - cross section, so as to form a needle system (9') with a substantially round cross section.

9. Catheter system according to Claim 5, in which the needle system (9') is formed by two straight coaxial needles of different length which are aligned with the axis of the catheter and in which the tip of the shorter needle with a larger diameter (9'b) is closed and suitably connected to the side surface of the longer needle (9'a).

10. Catheter system according to Claim 9, in which the shorter needle may be provided with several lateral discharge openings (111).

11. Catheter system according to Claim 5, in which the needle system (9) is formed by two helical needles of different length (9a, 9b) which are centred with respect to the axis of the catheter.

12. Catheter system according to Claim 11, in which the helical needles are arranged alongside each other and fixed with welds, the tip of the shorter needle being integral with and connected to the body of the longer needle.

13. Catheter system according to Claim 12, in which the helical needles (9a, 9b) have a cross section which is flattened and such that the needle system (9)

formed by it has a substantially round cross section.

14. Catheter system according to Claim 12, in which the helical needles (9a, 9b) enter into the catheter with straight sections arranged along the axis of the said catheter.

15. Catheter system according to Claim 9, in which the needle system (9) is formed by a pair of straight needles of different length which are coaxial with each other and aligned with the axis of the catheter and with the needle of greater length (9a) which terminates in a helical configuration.

16. Catheter system according to Claim 5, in which the needle system (9) is formed by a straight needle (9'a, 9'b) aligned with the axis of the catheter and by a helical needle (9b, 9a) arranged concentrically around the said central needle.

17. Catheter system according to Claim 16, in which the central straight needle (9'b) is shorter than the helical needle.

18. Catheter system according to Claim 16, in which the central straight needle (9'a) is longer than the helical needle so as to act as a centring device and rotational pivot for said helical needle.

19. Catheter system according to Claim 16, in which the helical needle (9a, 9b) enters into the catheter with a section located alongside the central needle (9'a, 9'b).

20. Catheter system according to Claim 16, in which the helical needle (9a, 9b) enters into the catheter with a section (A, B) distant from the central needle (9'a, 9'b) so as to prevent the rotation of the catheter when this section comes into contact with the wall of the myocardium.

21. Catheter system according to the preceding claims, in which the discharge openings (110, 111) of the lumina of the needle system are in different longitudinal positions of the needle itself, for example one at the tip of the needle system and the other upstream so as to supply separately fluids into the zone to be treated.

22. Catheter system according to the preceding claims, in which the needle system (9, 9') is electrically conducting.

23. Catheter system according to Claim 22, in which the electrically conducting needle system (9, 9') is lined with a thin film of electrically insulating material (45) over nearly the whole of its length, except for a suitable tip section which remains electrically conducting.

24. Catheter system according to Claim 23, in which the electrically insulating material (45) which partly lines the needle system (9, 9') comprises material known as "Parylene".

25. Catheter system according to Claim 22, in which the body of the catheter comprises at least a first longitudinal electrical conductor (14) connected at one end to the needle system (9, 9') and designed for connection at the external end to an external electrical apparatus (25).

26. Catheter system according to the preceding claims, particularly in the case where the needle system is wholly or partly of the helical type, characterized in that the body of the catheter (2) has an internal longitudinal structure, for example in the form of a meshwork braiding (102), which allows a twisting torque to be applied to the external end of the catheter and to ensure that this causes a corresponding rotation of the multilumen needle system (9, 9') fixed onto the terminal end of the said catheter.

27. Catheter system according to the preceding claims, in which the body of the catheter (2) is provided with at least a second longitudinal electrical conductor (15) which is electrically insulated from the conductor connected to the needle system and designed for connection of the external end to an external electrical apparatus (25) and for connection of its terminal end to an electrically conducting ring (16) located on the terminal end of the catheter and having the function of a reference electrode for all the operations where the needle system performs the function of a conductor of electrical impulses.

28. Catheter system according to the preceding claims, in which the said electrical conductors (14, 15) are seated, with suitable mutual insulation, in at least one longitudinal secondary lumen (7) in the body of the catheter (2).

29. Catheter system according to Claim 27, in which any one of the said electrical conductors (14, 15) may be constituted by the said twisting braiding (102) if made of electrically conducting material.

30. Catheter system according to the preceding claims, in which the external electrical apparatus (25) comprises a source of electric energy and electrical impulses.

31. Catheter system according to the preceding claims, in which the external electrical apparatus (25) comprises an apparatus for monitoring electro-physiological signals.

32. Catheter system according to the preceding claims, in which the external electrical apparatus (25) comprises an apparatus for measuring the electrical impedance.

33. Catheter system according to the preceding claims, in which the body

of the catheter comprises at least one filament-like, longitudinally extending, flexible conductor of ultrasound energy (42) which is acoustically coupled to the needle system (9, 9') and designed for connection at its external end to an external apparatus (25) supplying ultrasounds.

34. Catheter system according to the preceding claims, in which the body of the catheter comprises on its terminal end, at the base of the needle system (9, 9'), a stopping device (13) of the retractable type, with an external activating and deactivating control device (39), for limiting the penetration of the said needle system into the myocardium.

35. Catheter system according to Claim 34, in which the stopping system comprises a torus-shaped balloon (13) which is made of flexible and impermeable material and which, via a connection duct (113) of its internal chamber, is connected to the terminal end of a secondary longitudinal lumen (6) in the body of the catheter (2), the external end of which is designed for connection to an external system (39) for supplying and drawing fluid into and from the said balloon, respectively so as to fill it and activate it for the end-of-travel function which it must perform, or so as to neutralize it and ensure that it remains in the retracted condition, which is useful during insertion and extraction of the catheter.

36. Catheter system according to the preceding claims, in which the main lumina (3, 4) in the body of the catheter (2) are intended to convey the tracer fluid, for example having the form of a circle segment and being arranged opposite each other in specular fashion, these lumina having, arranged between them in a symmetrical manner, the axial secondary lumen (5) for receiving the spindle (8) guiding the catheter during use and there being provided, laterally with respect to this lumen, on the one hand the secondary lumen (6) for conveying the fluid filling and emptying the end-of-travel balloon (13) and, on the other hand, the secondary lumen (7) for receiving the electrical conductors (14, 15), the ends of which are connected to the

needle system (9, 9') and to the annular reference electrode (16).

37. Catheter system according to the preceding claims, in which the lumina of the catheter, except for the axial lumen (5), are closed at the external front end and the front section of the said catheter (2) having, mounted on it without the possibility of axial displacement, a rotating distributor or header (17) provided around the said catheter with annular chambers (26, 27, 28) which are isolated from each other and with respect to the exterior by annular sealing gaskets (29, 30, 31, 32) and into which chambers there lead, via respective radial holes, the two main lumina (3, 4) which are connected to the base connecting sections (109, 209) of the needle system and the secondary lumen (6) leading to the end-of-travel balloon (13), these chambers being provided with respective hollow connectors (33, 34, 35) for connection to flexible pipes (36, 37, 38) and to syringes (30, 40, 41) containing respectively the fluid for filling and emptying the said balloon, the tracer fluid and the therapeutic fluid.

38. Catheter system according to Claim 37, in which the distributor or header (17) is made of electrically insulating material and is provided with electrical conductors having brushes (23, 24) which allow an external electrical apparatus (25) to be connected to the electrical conductors (14, 15) which are connected to the needle system (9, 9') and to the annular reference electrode (16), the said brushes making contact with electrically conducting rings (21, 22) which are fixed onto the body of the catheter, arranged at a suitable distance from each other and insulated and fixed to the terminals of the said electrical conductors (14, 15) which emerge from the associated guide lumen (7) through lateral holes.

39. Catheter system according to Claim 33, characterized in that, according to a variation of embodiment, an ultrasound generator (44) is mounted on the terminal end of the catheter (2), said ultrasound generator (44) being integral with the base of one or both the needles of the needle system and connected to an electrical

circuit which passes through a secondary lumen of the catheter for connection to external power supply systems.

40. Catheter system according to the preceding claims, in which the body of the catheter (2) has, for example, an external diameter of about 7 French, that is about 2.1 mm.

41. Catheter system according to the preceding claims, in which the diameter of the helix of the needle system with at least one helical needle (9) is for example about 2 mm.

42. Catheter system according to the preceding claims, in which the length of the projecting section of the longer needle of the needle system does not exceed, for example, 5 mm, while the length of the projecting section of the shorter needle is for example about 2.5 mm.

43. Catheter system according to the preceding claims, in which the external diameter of each of the needles which form the needle system is for example about 0.30 mm.

44. Method for intramyocardiac therapeutic treatment using the catheter system according to the preceding claims, characterized by the following operational steps:

- inserting into the desired chamber of the heart, by means of conventional pre-formed or steerable catheter guides (1), a catheter (2) having two or more longitudinal lumina and provided at its terminal end with a multilumen needle system (9, 9'), the base connecting sections of which (109, 209) are connected to corresponding lumina of the catheter which are in turn connected at their external end to corresponding systems (40, 41) for releasing into a desired zone inside the myocardium fluids for therapeutic treatment and tracer fluids for external image

diagnostics systems;

- inserting the multilumen needle system (9, 9') into the myocardium at the desired point;

- checking and recording total and correct insertion of the needle system into the myocardium with injection, into the said myocardium, of a tracer fluid through the lumina of the catheter and the needle system which are intended to convey said fluid;

- releasing, in the part of the myocardium into which the multilumen needle system (9, 9') has been inserted, a therapeutic fluid via the lumina of the catheter and the needle which are intended to convey said fluid.

45. Method according to Claim 44, characterized in that the tracer fluid is discharged through the discharge opening (111) of the multilumen needle system which is closest to the base of the said needle system.

46. Method according to Claim 44, in which the said step of inserting the multilumen needle system (9, 9') into the wall of the myocardium at the desired point comprises a step involving rotation of the catheter and the associated needle mounted on the latter, in particular if of the helical type, after expansion and activation of the end-of-travel balloon (13) located at the base of the said needle system.

47. Method according to Claim 44, in which the said step of releasing therapeutic treatment fluids comprises the release of carrier systems for performing genic transfer to the heart cells, for example DNA plasmids.

48. Method according to Claim 44, characterized in that it comprises a step involving connection of the electrical conductor associated with the multilumen needle system (9, 9') of the catheter to an external apparatus (25) which generates electric energy and which, by means of electrical impulses synchronized with the

beat R of the spontaneous activity of the heart, reinforces transfer of the DNA plasmids into the cells of the perfused myocardium.

49. Method according to Claim 44, characterized in that it involves a step involving activation of the ultrasound conductor (42) or the ultrasound generator (44) associated with the needle system (9, 9') in order to reinforce the transfer of the DNA plasmids into the cells of the perfused myocardium.

50. Method according to Claim 44, characterized in that it comprises a step involving checking of the state of penetration of the multilumen needle system (9, 9') into the myocardium, by connecting the electrical conductor associated with the said needle system to an external apparatus (25) for monitoring the intramyocardiac electrocardiograph.

51. Method according to Claim 44, characterized in that it comprises a step involving checking of the state of penetration of the needle into the myocardium, by connecting the electrical conductor associated with the multilumen needle system (9, 9') to an external apparatus (25) for measuring the bioelectric impedance.

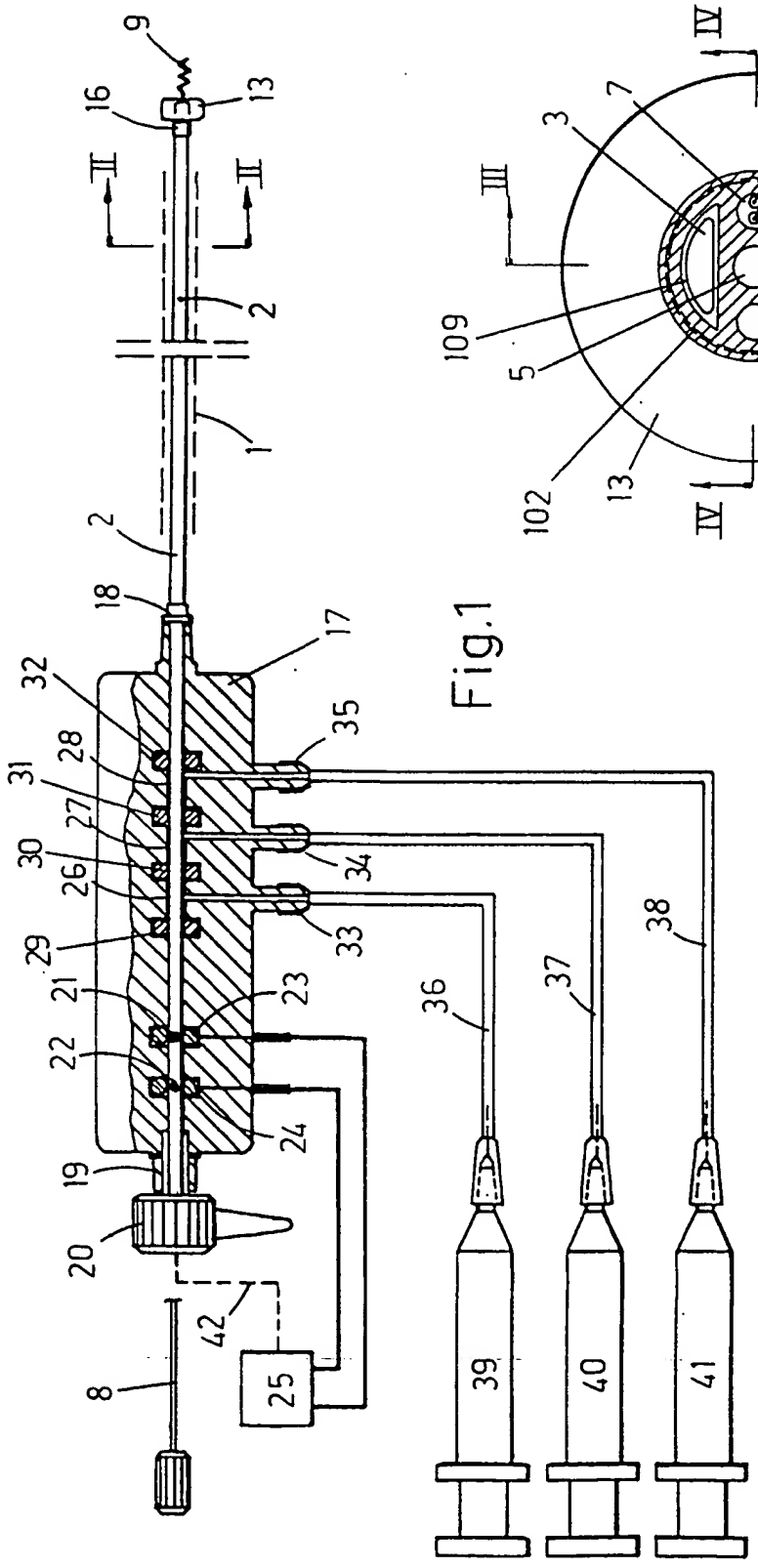

Fig.1

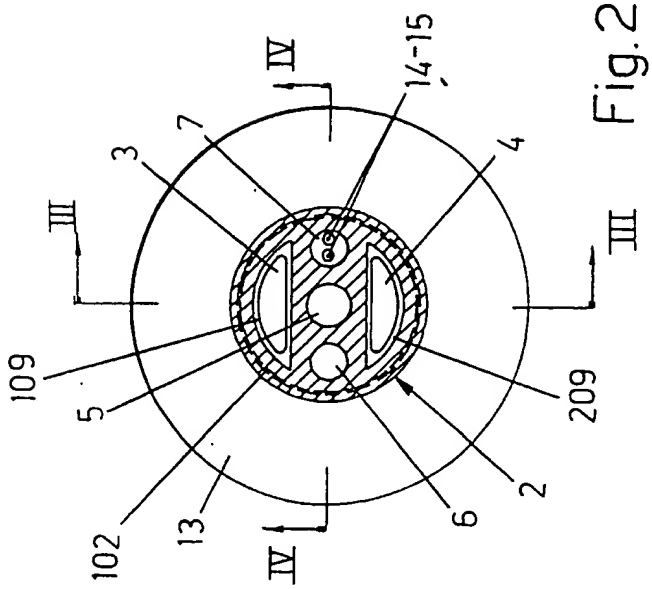

Fig.2

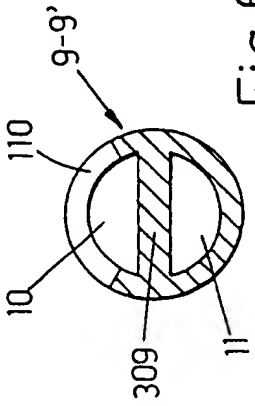

Fig.6

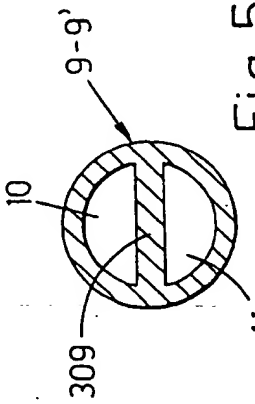

Fig.5

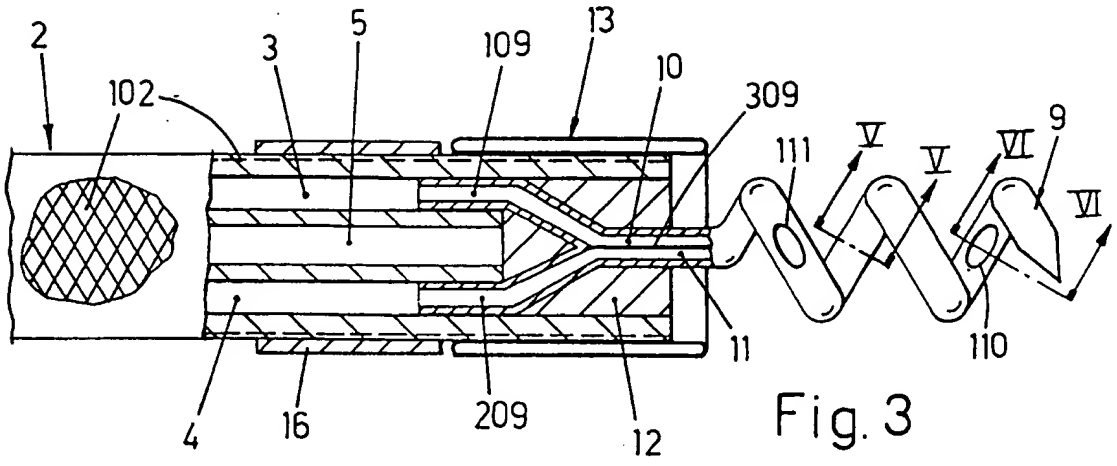

Fig. 3

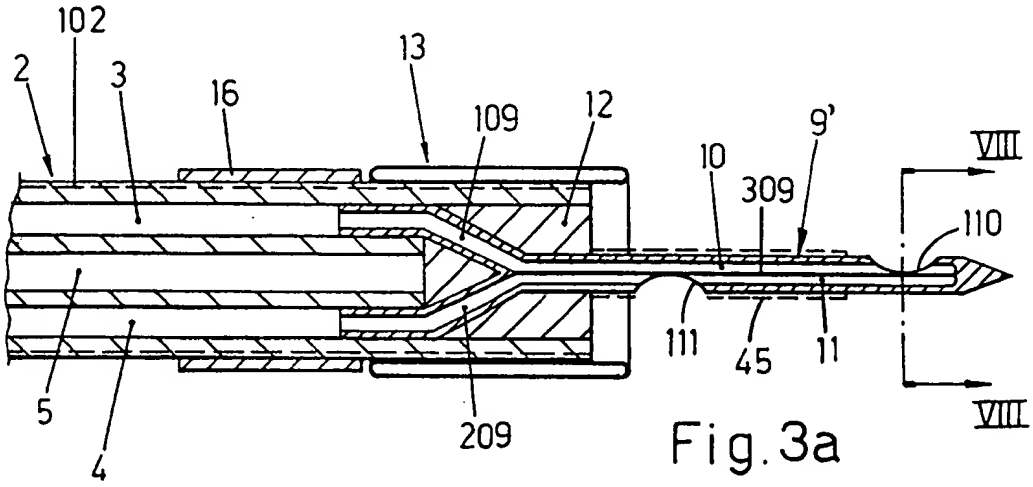

Fig. 3a

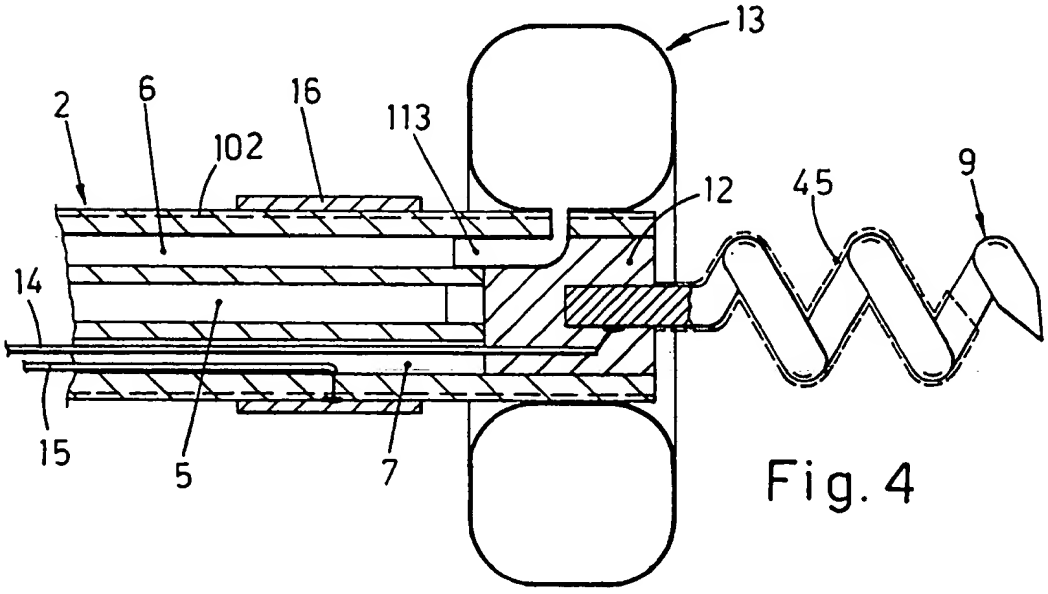

Fig. 4

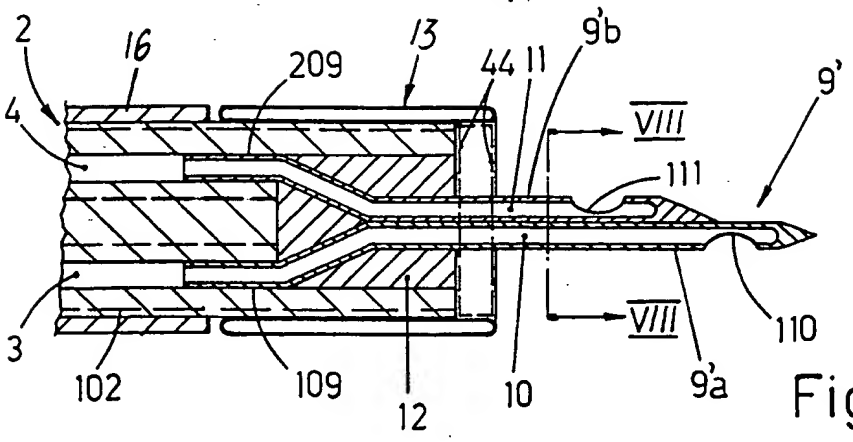

Fig. 7

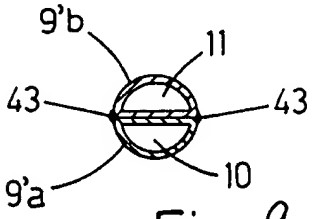

Fig. 9

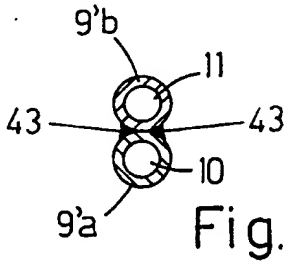

Fig. 8

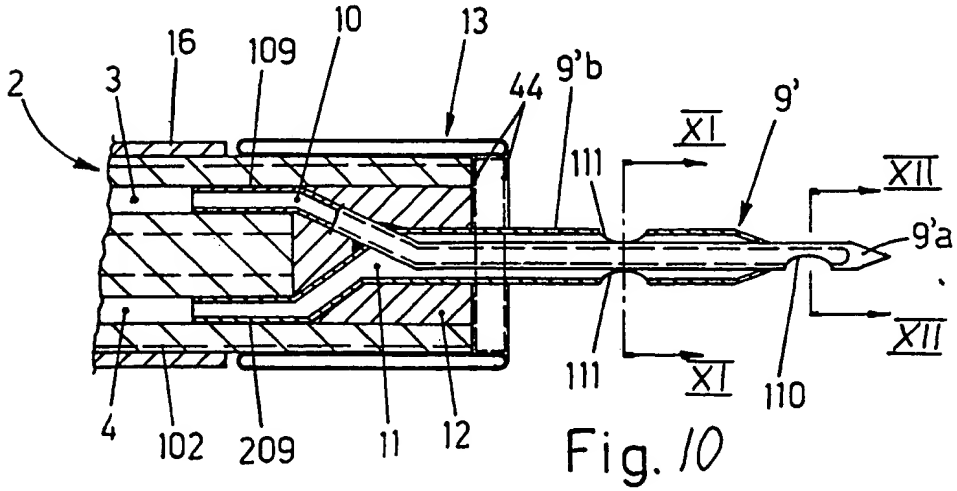

Fig. 10

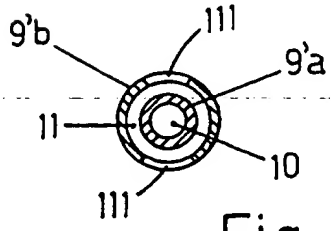

Fig. 11

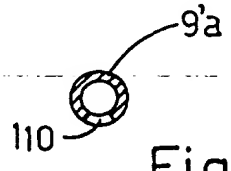

Fig. 12

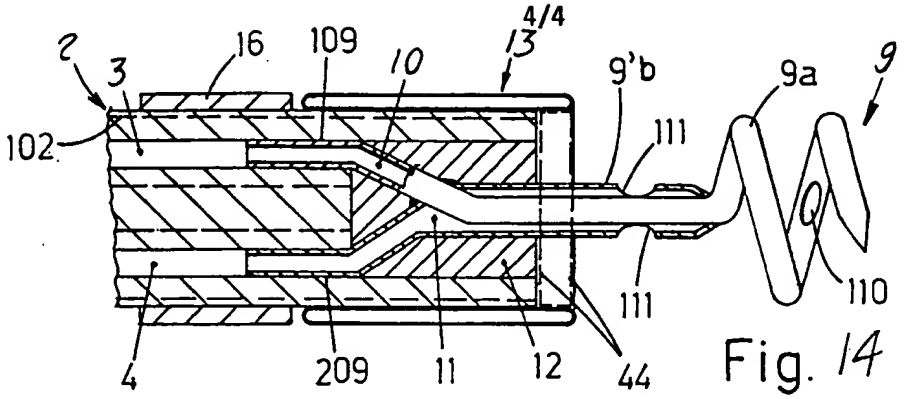

Fig. 14

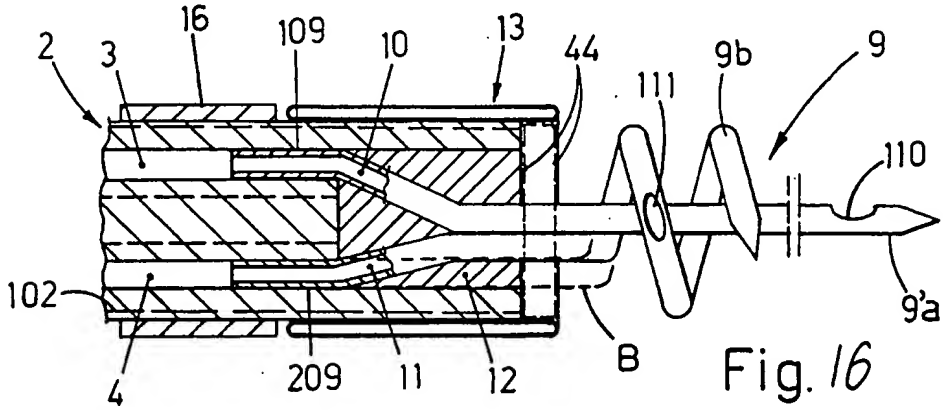

Fig. 16

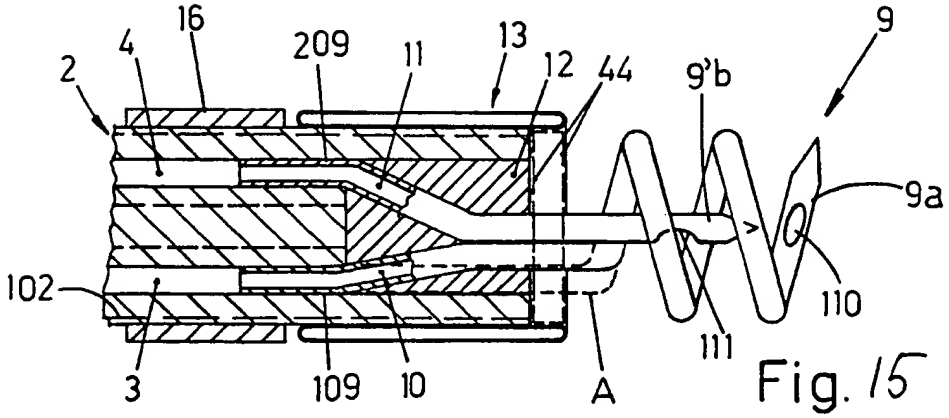

Fig. 15

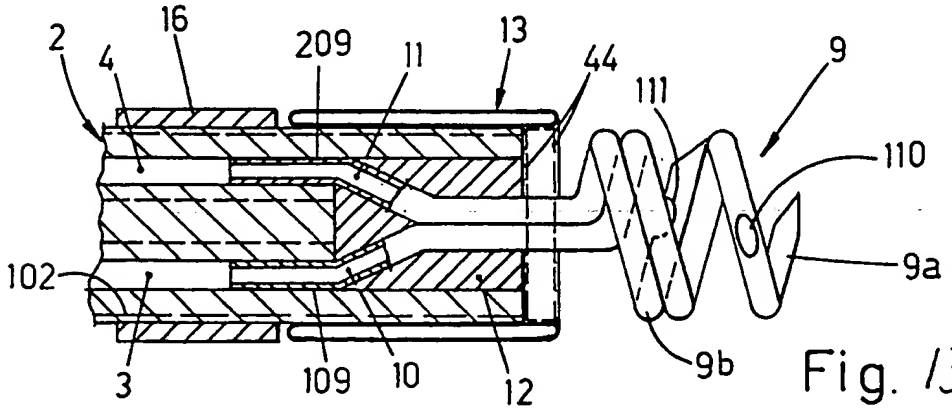

Fig. 13

INTERNATIONAL SEARCH REPORT

Inte...ional Application No
PCT/EP 99/08686

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N1/05 A61M25/00 A61B18/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M A61N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y A	US 5 531 780 A (VACHON) 2 July 1996 (1996-07-02) abstract column 1, line 12 - line 22 column 2, line 57 -column 3, line 14 column 3, line 62 -column 4, line 29; figures 1,4,5,8-12	1-33,36, 39-43 34,35, 37,38
Y	US 5 322 510 A (LINDNER ET AL.) 21 June 1994 (1994-06-21) abstract; figures 5,8-11	1-25, 30-32, 36,40-43
Y	EP 0 629 416 A (CORDIS EUROP) 21 December 1994 (1994-12-21) abstract; figures 1-5	26-29
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
2 March 2000	10/03/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Michels, N

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INTERNATIONAL SEARCH REPORT

Inter. ...onal Application No
PCT/EP 99/08686

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 808 607 A (SULZER OSYPKA GMBH) 26 November 1997 (1997-11-26) abstract; figure 7	33,39
A	US 5 084 016 A (FREEMAN ET AL.) 28 January 1992 (1992-01-28) abstract; figures 1,9	1,34,35
A	US 5 609 151 A (HOEY ET AL.) 11 March 1997 (1997-03-11) abstract; figures 1,2,4-7,12	1,37,38
X,P	WO 99 39624 A (BIOSENSE INC) 12 August 1999 (1999-08-12) * The Whole Document *	1-43
A	US 5 797 870 A (MARCH ET AL.) 25 August 1998 (1998-08-25)	
A	US 5 431 649 A (HOEY ET AL.) 11 July 1995 (1995-07-11)	

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 99/ 08686

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 44-51
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

information on patent family members

Intern. ...onal Application No
PCT/EP 99/08686

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